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Experimental Studies on the Lymphatics of the Esophagus from the Surgical Point of View

by

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INTRODUCTION

The results of surgical treatment of esophageal cancer have been unsatisfactory and discouraging in spite of recent surgical progress. According to the statistics in 1966, the mean resectability of esophageal cancer in our country was 46.0%[2] and the five years' survival rates in such patients were only 2 % in the upper two thirds of the thoracic esophagus, 5.6% in the lower third, and 6.6% in the esophagocardiac region.[1] On the other hand, the over-all resectability was 43 % in the series of Lahey Clinic Foundation in 1967[8]. In many cases of other countries during the past 10 years, it was found that 4 to 14.9% of patients undergoing resection lived five years or longer[18)23)27)30)].

Some difficulties encountered by the radical treatment of this carcinoma are the occurrence of tumor metastasis and extensive involvement of adjacent organs at a relatively early stage. When the patient is ready for operation, 67 to 80% of them have metastatic spread in regional lymph nodes[9)12)28)].

There have been many reports about the relationship between the thoracic duct and the esophagus[40)], the stomach[45)] or the retroperitoneal lymphatic systems[22)]. For instance, EFSKIND and HELSINGEN found tumor cells in lymph from the thoracic duct during operation in about 60% of cases[18)].

In other words, this means that the esophagus has a close relation with the thoracic duct. Therefore, investigations on the lymphatic system of the esophagus using RIHSA (radioactive iodinated human serum albumin) from clinical and experimental viewpoints would be significant for elucidating the features of lymphatic dissemination of esophageal cancer.

MATERIALS AND METHODS

Mongrel dogs weighing about 10 kg were anesthetized with pentobarbital (25 mg per kg). Through a left paramedian incision in the cervical region, the thoracic duct was

dissected and ligated just proximal to the jugular-subclavian junction. A polyethylene tube (1.33 mm in diameter) was cannulated into the dilated proximal portion of the thoracic duct. The test solution of 2 ml, 50 μc RIHSA mixed with Evans Blue was injected into the cervical (Ce), upper (Iu), middle (Im), and lower (Ei) portions of the thoracic esophagus using a long needle with a tuberculin syringe (0.15 × 50 cm) under a direct view through the esophagoscope (Fig. 1).

In the abdominal esophagus (Ea), RIHSA solution was injected directly into the wall after laparotomy.

One ml of thoracic duct lymph was collected into heparinized test tubes every 15 minutes for the first hour, and every 30 minutes for the following two hours. The radioactivities of these specimens of lymph and 1 ml of the venous blood were measured by a scintillation counter of well-type. Then, the dogs were bled to death from the femoral artery, and thereafter, all of the cervical, the thoracic and the upper abdominal lymph nodes associated with the esophagus were collected. Direct counts on the lymph nodes were made by placing the specimens in a test tube. The results were recorded as counts per minute (c p m.) and were also expressed as a percentage of the count of 1 g specimen at the injection site.

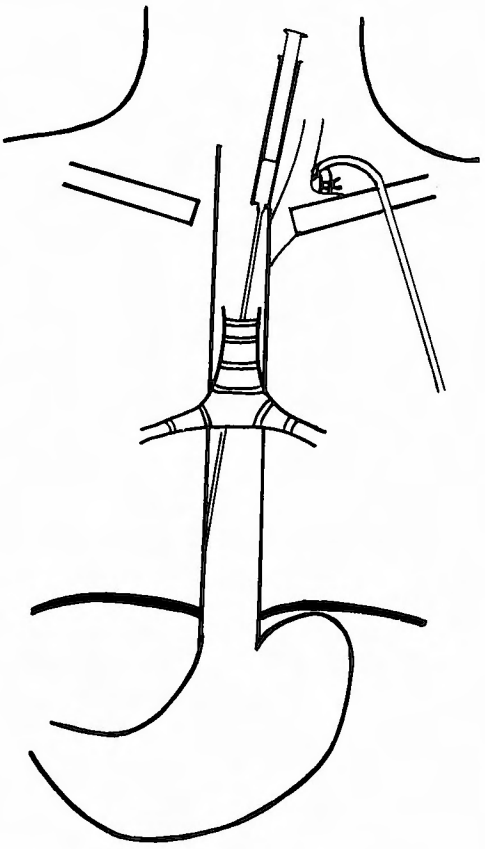

Fig. 1 Diagram showing technique of injection into the esophageal wall using a long needle after drainage of the thoracic duct.

RESULTS

1. Experiments with RIHSA injection into the esophagus.

RIHSA in lymph of the thoracic duct was already found 15 minutes after the injection (Tab. 1, Fig. 2). When I^{131}-albumin was injected into the abdominal esophagus, the radioactivity in the thoracic duct lymph increased rapidly for 60 minutes, then decreased gradually, but increased again 150 minutes after the injection.

Table 2 represents the relationship between the esophagus and the regional lymph nodes. These results showed a close relationship between the esophagus and the thoracic duct, but some differences were found among five anatomical parts of the esophagus.

As one might expect, when the cervical portion was injected, the lymph nodes in the upper thorax showed a high count. All nodes in the mediastinum and even the upper abdominal nodes demonstrated high activities following injection into the wall of the thoracic esophagus. When the abdominal esophagus was injected, the thoracic, especially the middle

Table 1 Lymph radioactive values of the thoracic duct following RIHSA injection into the esophagus (CPM).

Ce : Cervical portion of the esophagus
Iu : Upper thoracic portion of the esophagus
Im : Mid-thoracic portion of the esophagus
Ei : Lower thoracic portion of the esophagus

Injection site of the esophagus	Min. / Dog	15	30	45	60	90	120	150	180
Ce	No. 7	212	206	200	304	387	516	496	481
	No. 9	90	100	120	226	280	325	337	377
	No. 10	188	220	173	210	350	300	334	373
	Mean	151	163	189	235	327	369	377	398
Iu	No. 12	113	204	318	627	737	1196	1500	1315
	No. 13	55	160	270	567	607	816	1384	1764
	No. 16	130	201	784	1682	1214	1087	1512	1375
	Mean	99	188	457	959	852	1033	1465	1488
Im	No. 20	86	343	592	956	1374	2111	2607	2327
	No. 21	62	309	549	1904	2561	2860	3427	3281
	No. 23	42	352	581	744	759	883	1200	1422
	Mean	63	217	574	1201	1565	1951	2411	2343
Ei	No. 25	39	203	369	413	348	500	669	934
	No. 26	31	237	1894	2400	2843	2630	2829	4541
	No. 29	16	214	274	226	300	288	334	452
	Mean	29	218	846	1013	1164	1139	1277	1976

Table 2 Distribution of radioactivity following RIHSA injection into the esophagus

Specimen \ Dog No. and injection site	Per cent count				
	10 Ce	13 Iu	21 Im	28 Ei	33 Ea
Injection site	100	100	100	100	100
Right retropharyngeal node	10.4	0.4	0	0	0
Left retropharyngeal node	10.1	0.4	0	0	0
Left deep cervical node	—	—	0	0	0.5
Superior mediastinal node	—	50.8	0.4	5.6	1.0
Paratracheal node	—	—	—	—	—
Right tracheobronchial node	2.0	5.1	0.8	0.3	8.0
Middle tracheobronchial node	1.0	10.1	8.1	11.8	57.5
Left tracheobronchial node	2.0	3.4	5.6	3.9	0
Nodes along the left gastric artery	0.1	—	—	—	3.6
Splenic node	—	—	0.1	1.9	2.0
Hepatic node	—	0	—	0.2	23.7

tracheobronchial (the tracheal bifurcation) nodes showed much activity.

2. Experiments with RIHSA injection after removal of the lymph nodes in the upper abdomen.

All of the lymph nodes along the lesser curvature and spleno-portal vein, and at the splenic or hepatic hili etc. were removed in dogs, and one or two weeks later, laparotomy was performed again. Fifty μc RIHSA was injected directly into the abdominal esophagus, and one ml of lymph in the thoracic duct, and blood in the femoral vein was collected to count the radioactivities (Tab. 3, Fig. 3 and 4).

After extirpation of nodes, the activity in lymph of the thoracic duct was significantly lower than that of the control group, however, in the venous blood it was higher than the values of the control group. Table 4 represents the per cent count of the regional nodes in the cervical and thoracic regions. They showed lower values than those of the control group. The marked reduction of I^{131}-albumin in the thoracic duct lymph, not in the venous blood, suggests that venous vessels take a preponderant role in draining off the lymph from the injection site of the esophagus after devasation or severance of lymphatics.

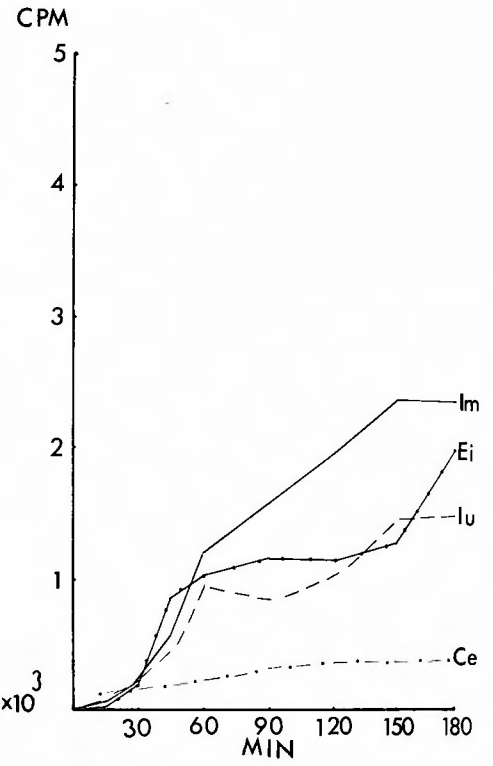

Fig. 2 Radioactivity in thoracic duct lymph following injection of RIHSA into the wall of Ce, Iu, Im and Ei.

Table 3 Radioactive values following RIHSA injection into the abdominal esophagus (CPM)

	Radioactivity in thoracic duct lymph						Radioactivity in venous blood					
	Control				After removal of lymph nodes		Control				After removal of lymph nodes	
No. / Min	30	33	34	Mean	35 1wk	36 2wks	30	33	34	Mean	35 1wk	36 2wks
15	13028	778	196	4667	80	98	825	413	420	553	1310	979
30	59143	4280	1966	21796	637	1170	1028	525	423	659	1898	1378
45	71020	9631	7250	29303	2042	5212	1113	618	500	744	2156	1544
60	80867	17196	11287	36450	5604	5820	1222	581	640	814	2500	2076
90	58953	28374	18750	35359	4197	4624	1426	746	618	730	3280	3134
120	48273	28260	14823	30452	4207	3297	1935	883	892	1237	3788	3876
150	41858	26538	13096	27161	3284	4834	3070	1128	953	1717	3826	4522
180	56187	21823	13197	30402	4027	8005	2780	1329	976	1695	3394	5187

3. Experiments with RIHSA injection after ligation of the left gastric artery with removal of the lymph nodes in the upper abdomen.

Ligation of the left gastric artery at the root of the celiac trunk was performed in

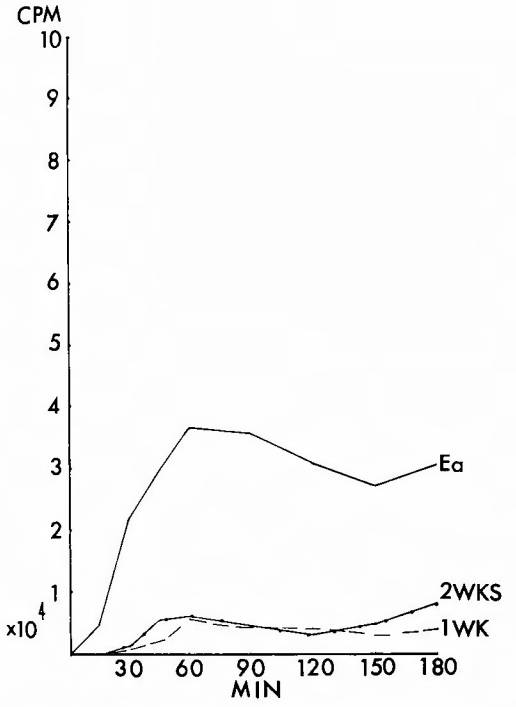

Fig. 3 Radioactivity in thoracic duct lymph following injection of RIHSA into the abdominal esophagus (Ea) and 1 wk. or 2 wks. after removal of the lymph nodes of the upper abdomen.

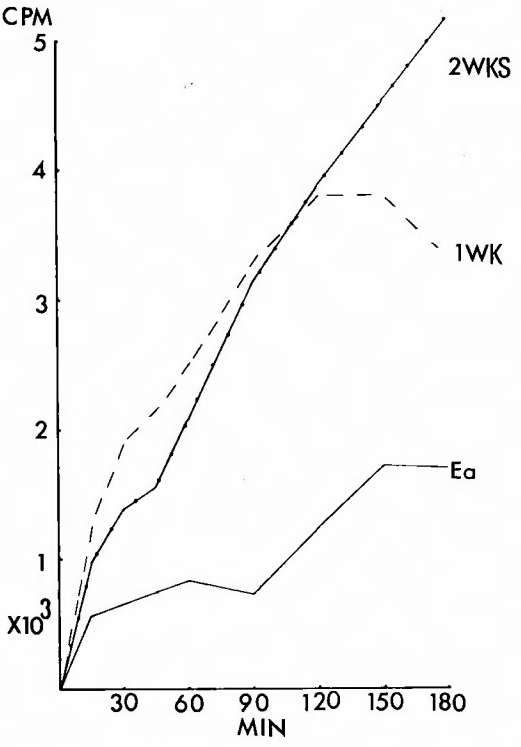

Fig. 4 Radioactivity in venous blood following injection of RIHSA into the abdominal esophagus and 1 wk. or 2 wks. after removal of the lymph nodes of the upper abdomen.

Table 4 Distribution of radioactivity following RIHSA injection into the abdominal esophagus after extirpation of lymph nodes

Specimen \ Dog No.	Per cent count	
	35 (1wk)	36 (2wks)
Injection site	100	100
Right retropharyngeal node	0	0
Left retropharyngeal node	0	0
Left deep cervical node	0	0
Superior mediastinal node	0.2	0.4
Paratracheal node	—	1.6
Right tracheobronchial node	0.8	0.4
Middle tracheobronchial node	2.0	12.4
Left tracheobronchial node	1.0	3.8

addition to removal of the lymph nodes in the upper abdomen. Radioactivities of I^{131}-albumin were measured in the thoracic duct lymph, the venous blood and the regional lymph nodes, from 2 to 4 weeks postoperatively (Tab. 5 and 6, Fig. 5 and 6). As indicated in Fig. 5 and 6, the appearance of I^{131}-albumin both in thoracic duct lymph and in venous blood decreased 2 weeks after the procedures. On the contrary, the ap-

Table 5 Radioactive values following RIHSA injection into the abdominal esophagus after ligation of the left gastric artery with removal of the lymph nodes of the upper abdomen (CPM)

Min. \ Dog No.	Radioactivity in thoracic duct lymph			Radioactivity in venous blood		
	82 (2wks)	83 (3wks)	46 (4wks)	82 (2wks)	83 (3wks)	46 (4wks)
15	159	5094	79	554	240	705
30	261	94300	18011	748	402	992
45	1009	103673	46542	807	678	1158
60	1916	104702	65596	867	880	1400
90	3257	90324	73832	930	1590	1714
120	6452	42102	79543	942	1926	1733
150	4802	51699	82689	1026	2400	2052
180	9116	39266	97389	1060	2648	2328

Table 6 Distribution of radioactivity following RIHSA injection into the abdominal esophagus after ligation of the left gastric artery with removal of the lymph nodes of the upper abdomen

Specimen \ Dog No.	Per cent count		
	82 (2wks)	83 (3wks)	46 (4wks)
Injection site	100	100	100
Right retropharyngeal node	0	0	0
Left retropharyngeal node	0	0	0
Left deep cervical node	0	0.2	0
Superior mediastinal node	0	3.3	6.5
Paratracheal node	0	2.7	0
Right tracheobronchial node	0	0.5	0
Middle tracheobronchial node	0	14.9	3.5
Left tracheobronchial node	0	3.2	1.0

pearance of RIHSA remarkably increased 3 weeks after the procedures. It suggests that the communication between the esophagus and the thoracic duct regenerated and began to function through new channels 3 weeks after destruction of the lymphatic vessels."

The per cent count of the regional lymph nodes exhibited zero in the 2nd postoperative week, but a large amount of radioactivities, for instance, in the middle tracheobronchial node were measured in the 3rd postoperative week (Tab. 6).

4. Experiments with RIHSA injection after paraffin-blockade of the esophageal lymphatics.

The lymphatics of the esophagus were blocked by injecting 5 ml of paraffin (melting point : 42°C) into each of the anterior, posterior, right-, and left-sided walls of the esophagus with a long needle. Following injection of RIHSA into the esophagus distal to the blocked site 2 weeks after the procedure, the appearance of I^{131}-albumin in the thoracic duct lymph was delayed for 90 minutes (Tab. 7, Fig. 7). However, count per minute in the venous blood was higher as compared with that in the thoracic duct lymph except in the lower portion of the esophagus (Tab. 7, Fig. 8). This might be attributed to the reappearance of RIHSA from the circulating blood into the thoracic duct lymph. It is very difficult for RIHSA to be injected correctly distal to the blocked portion, there-

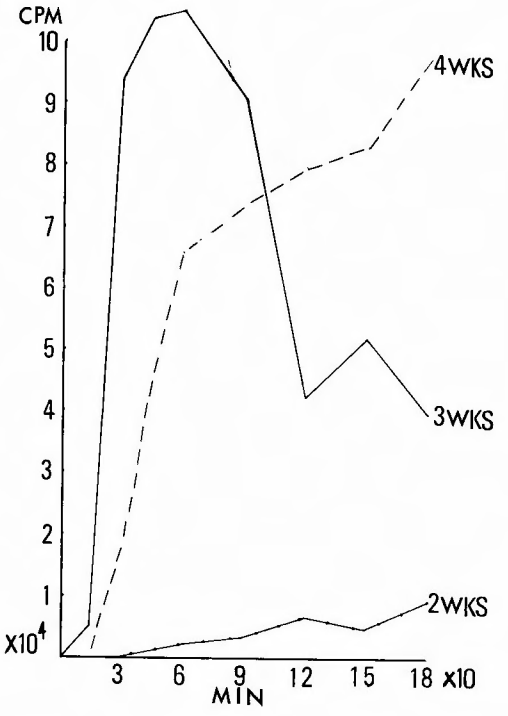

Fig. 5 Radioactivity in thoracic duct lymph following injection of RIHSA into the abdominal esophagus 2~4 wks. after ligation of the left gastric artery with removal of the lymph nodes of the upper abdomen.

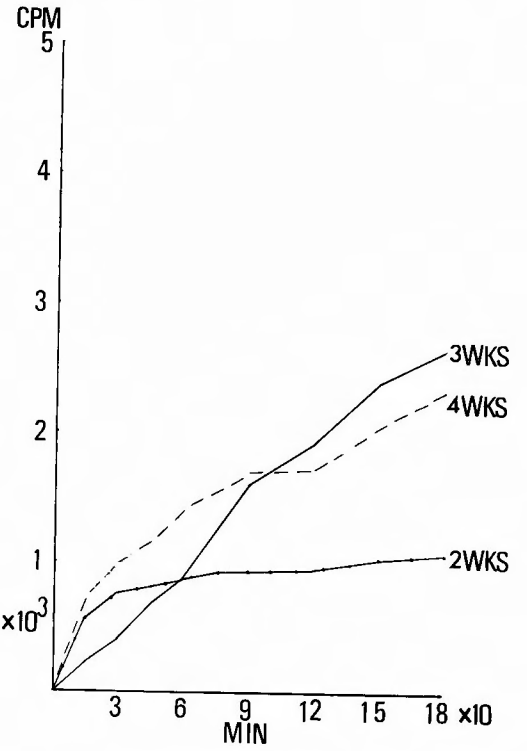

Fig. 6 Radioactivity in venous blood following injection of RIHSA into the abdominal esophagus 2~4 wks. after ligation of the left gastric artery with removal of the lymph nodes of the upper abdomen.

Table 7 Radioactive values following RIHSA injection into the esophagus 2 weeks after blocking with paraffin (CPM)

Min. \ Dog No. and blocked site	Radioactivity in thoracic duct lymph			Radioactivity in venous blood		
	38 Iu	51 Im	58 Ei	38 Iu	51 Im	58 Ei
15	98	64	18	283	302	133
30	124	248	99	488	327	142
45	194	266	96	619	439	148
60	243	297	127	985	482	226
90	406	309	182	1804	708	307
120	826	353	1482	2106	952	483
150	1083	472	2281	2512	1269	723
180	1279	636	1446	3024	1646	960

fore, the data obtained in the lower portion of thoracic esophagus might not be authentic. Per cent count of the lymph nodes showed an increase in the nodes under the diaphragm (Tab. 8). It is reasonable to presume that retrograde lymph channels developed after the blockade of lymph flow in the esophagus.

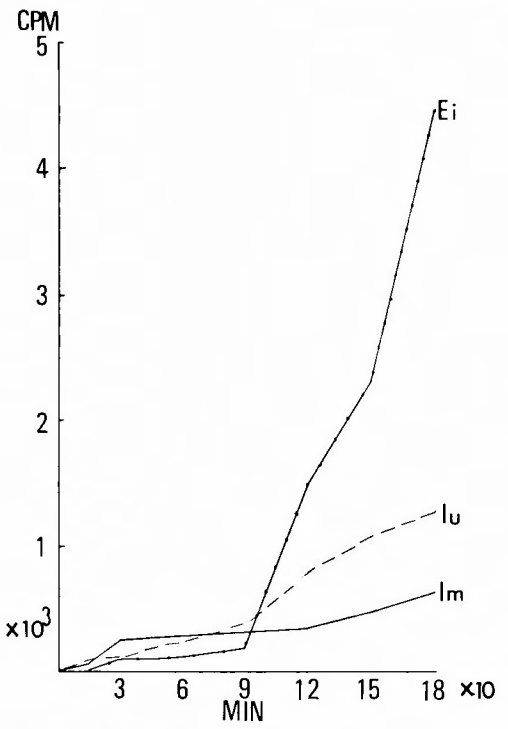

Fig. 7 Radioactivity in thoracic duct lymph following injection of RIHSA into the esophagus distally 2 weeks after blocking with paraffin.

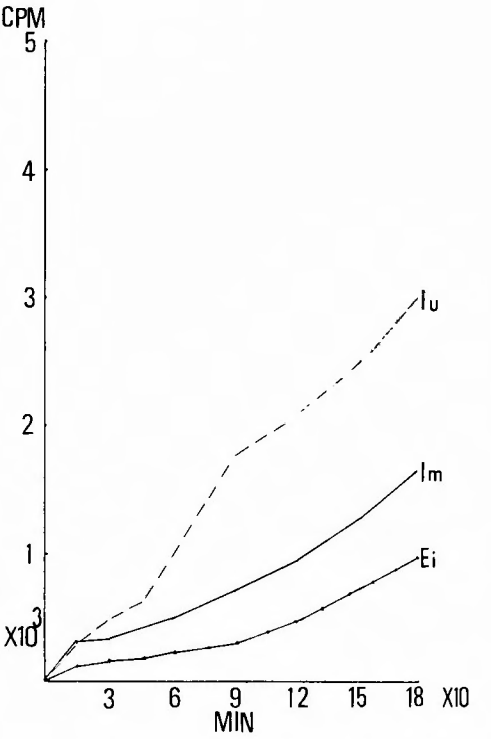

Fig. 8 Radioactivity in venous blood following injection of RIHSA into the blocked esophagus distally.

Table 8 Distribution of radioactivity following RIHSA injection into the esophagus 2 weeks after blocking with paraffin

Specimen \ Dog No. and blocked site	Per cent count		
	38 Iu	51 Im	58 Ei
Injection site	100	100	100
Right retropharyngeal node	0	0.3	0.3
Left retropharyngeal node	0	0.5	0
Left deep cervical node	0	0.6	—
Superior mediastinal node	2.8	0.5	34.3
Paratracheal node	6.4	—	11.1
Right tracheobronchial node	0.1	1.0	3.0
Middle tracheobronchial node	51.5	11.0	12.5
Left tracheobronchial node	10.7	0.3	—
Cardiac node	—	—	7.2
Nodes along the left gastric artery	0	—	—
Splenic node	—	5.7	0.9
Hepatic node	0.1	0.2	0.3

5. Experiments with RIHSA injection following thoracic vagotomy.

After drainage of the thoracic duct lymph under the controlled respiration with a respirator (20 times per minute), right tharacotomy was performed through the sixth intercostal space. Thereafter, both of the vagal nerves were severed at the height of the bifurcation. RIHSA was injected into the esophagus at the same level or the lower thoracic esophagus. The relations between the middle or lower thoracic portion of the esophagus and the thoracic duct lymph or the venous blood are illustrated in Table 9, and Figures 9 and 10. Table 10 shows the results of the per cent count in the regional lymph nodes.

As thoracotomy will greatly influence the dynamics of respiration, and intrathoracic pressure, the lymph flow in the thoracic duct will be changed. Table 11 and Figures 11 and 12 show the results in the control group which had undergone thoracotomy only. After vagotomy the appearance of RIHSA in the thoracic duct lymph following injection into the middle thoracic portion decreased remarkably as compared with that of the control group. On the other hand, no remarkable difference in the venous blood was found between these two groups, although the appearance of RIHSA in the venous blood seemed

Table 9 Radioactive values following RIHSA injection into the thoracic esophagus after vagotomy (CPM)

Dog No. and injection site / Min.	Radioactivity in thoracic duct lymph		Radioactivity in venous blood	
	77 (Im)	71 (Ei)	77 (Im)	71 (Ei)
15	102	167	403	1060
30	487	23179	517	1150
45	3053	71459	469	1558
60	3537	53666	544	1920
90	9592	46340	1338	2188
120	18801	16425	1390	2593
150	22237	19395	1256	2916
180	25619	21945	1486	3557

Table 10 Distribution of radioactivity following RIHSA injection into the esophagus after vagotomy

Specimen / Dog No. and injection site	Per cent count	
	77 (Im)	71 (Ei)
Injection site	100	100
Right retropharyngeal node	0	0
Left retropharyngeal node	0	0
Superior mediastinal node	0.3	0.1
Paratracheal node	0.2	0.4
Right tracheobronchial node	0.3	0
Middle tracheobronchial node	0.4	1.4
Left tracheobronchial node	0.6	0.2
Nodes along the left gastric artery	0	—
Splenic node	0.3	0.9
Hepatic node	0	0

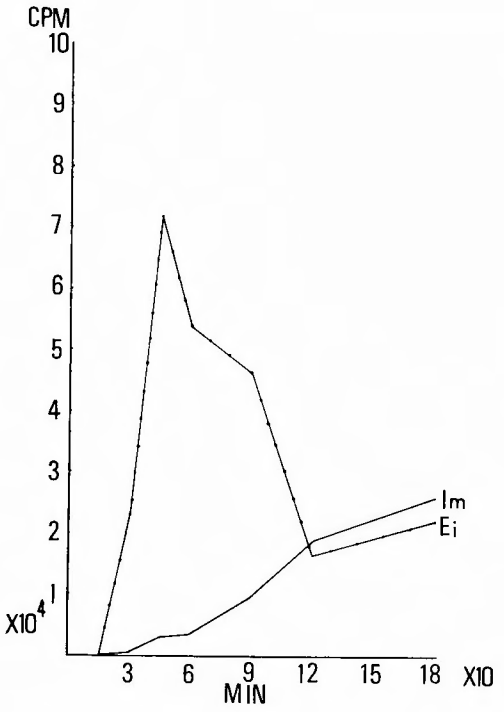

Fig. 9 Radioactivity in thoracic duct lymph following injection of RIHSA into the esophagus after severing the vagal nerves.

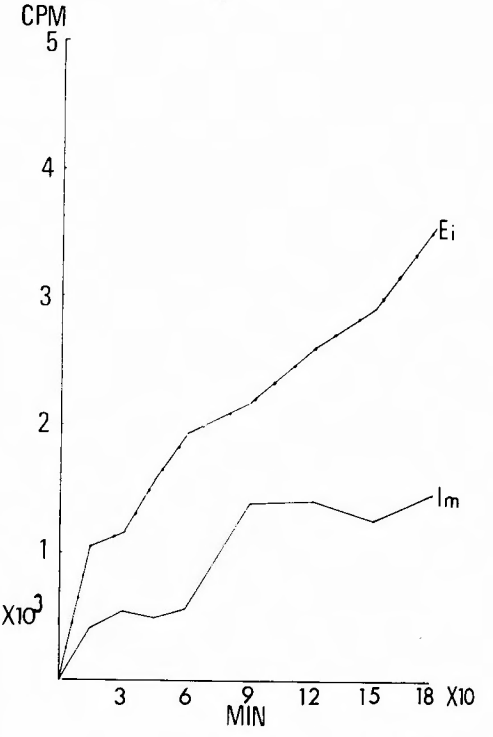

Fig. 10 Radioactivity in venous blood following injection of RIHSA into the esophagus after vagotomy.

Table 11 Radioactive values following RIHSA injection into the thoracic esophagus after thoracotomy (CPM)

Dog No. and injection site	Radioactivity in thoracic duct lymph			Radioactivity in venous blood		
Min.	78 Iu	76 Im	75 Ei	78 Iu	76 Im	75 Ei
15	184	398	13622	1779	439	552
30	562	35316	37370	2176	598	775
45	801	24677	41354	2372	1404	1154
60	1418	18188	63137	3394	850	1513
90	2142	70401	25750	3886	1043	3665
120	2637	71454	15897	5090	1145	4405
150	3805	95216	16027	5428	1340	4974
180	4650	81672	14356	4780	1658	6156

to reduce for 60 minutes after vagotomy and elevate slightly 90 minutes later. After vagotomy the appearance of RIHSA in the thoracic duct lymph and the venous blood following injection into the lower thoracic esophagus tended to increase, but fell below the control values in the venous blood after 60 minutes (Tab. 9, Fig. 10). No significant predisposition was found in the per cent count of the regional lymph nodes (Tab. 10).

Table 12 Distribution of radioactivity following RIHSA injection into the thoracic esophagus after thoracotomy

Dog No. and injection site / Specimen	Per cent count		
	78 (Iu)	76 (Im)	75 (Ei)
Injection site	100	100	100
Right retropharyngeal node	0	0	0
Left retropharyngeal node	0	0	0
Superior mediastinal node	2.0	0.3	1.0
Paratracheal node	0	0.6	0.2
Right tracheobronchial node	24.0	0.1	0
Middle tracheobronchial node	9.2	1.1	2.0
Left tracheobronchial node	3.3	0.7	1.0
Nodes along the left gastric artery	—	—	—
Splenic node	0	22.5	1.0
Hepatic node	0	0.1	0.2

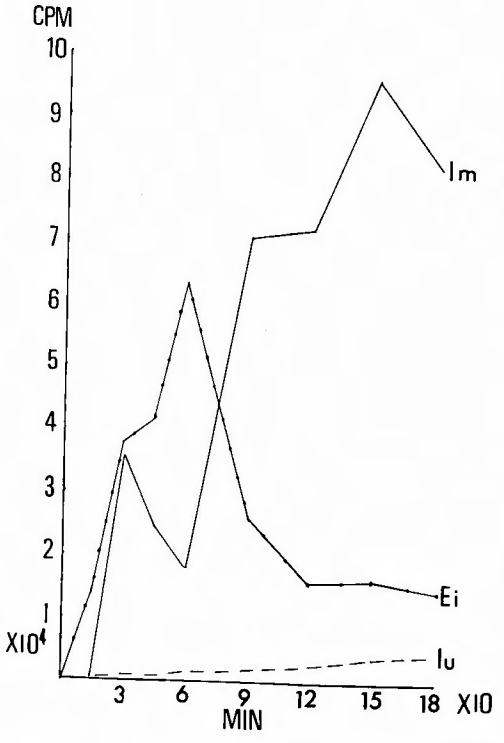

Fig. 11 Radioactivity in thoracic duct lymph following injection of RIHSA into the esophagus after thoracotomy.

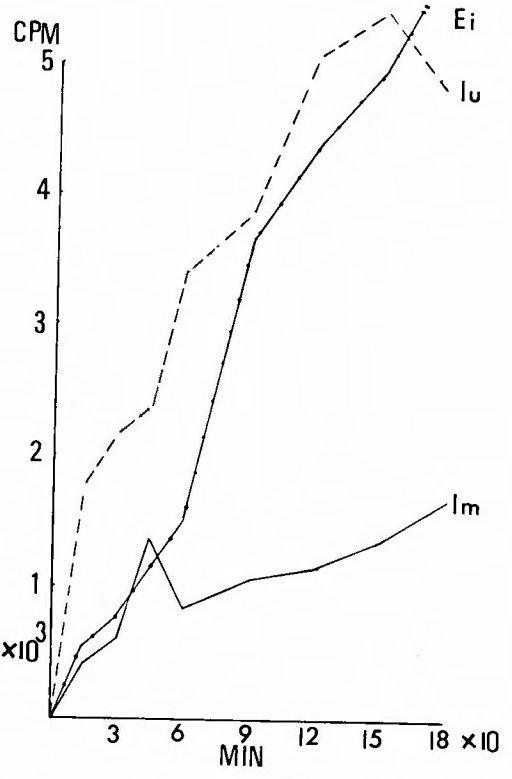

Fig. 12 Radioactivity in venous blood following injection of RIHSA into the esophagus after thoracotomy.

6. Experiments with RIHSA injection after ligation of the azygos and the intercostal veins.

The right thoracotomy was carried out through the sixth intercostal space. The azygos vein was ligated at the level where it entered into the superior vena cava. The intercostal veins on both sides, situated from the same level to the tenth intercostal space, were also ligated. Then, 50 μc of RIHSA was injected into the esophagus after drainage of the thoracic duct. No remarkable change was observed in the count of the lymph following injection into the upper thoracic portion of the esoghagus. However, it resulted in a marked reduction in the counts of the lymphs following injection into the middle or the lower thoracic portion of the esophagus for 120 minutes (Tab. 13, Fig. 13 and 14). Generally, the appearance of RIHSA in the venous blood was lowered below that of the control (Fig. 14). There is no doubt that ligation of the azygos and the intercostal veins has same effects on the venous flow and the lymph flow in the esophagus.

Table 13 Radioactive values following RIHSA injection into the thoracic esophagus after ligation of the azygos and the intercostal veins (CPM)

Dog No. and injection site	Radioactivity in thoracic duct lymph			Radioactivity in venous blood		
Min.	69 Iu	67 Im	68 Ei	69 Iu	67 Im	68 Ei
15	1317	178	139	192	304	300
30	3279	391	1158	310	647	425
45	2023	569	3138	598	789	482
60	1891	855	7369	896	816	613
90	2550	1589	9263	1540	1260	1045
120	2991	3590	17795	1842	1617	1892
150	3040	6237	30986	2360	2029	3015
180	3968	11510	38836	2960	2541	5596

Table 14 Distribution of radioactivity following RIHSA injection into the thoracic esophagus after ligation of the azygos and the intercostal veins

Dog No. and injection site / Specimen	Per cent count		
	69 (Iu)	67 (Im)	68 (Ei)
Injection site	100	100	100
Right retropharyngeal node	0	0	0.5
Left retropharyngeal node	0	0	0.7
Superior mediastinal node	6.3	4.5	26.0
Paratracheal node	0.6	0.8	—
Right tracheobronchial node	0	23.7	8.0
Middle tracheobronchial node	0.7	57.1	28.4
Left tracheobronchial node	4.5	18.0	8.7
Nodes along the left gastric artery	—	0.7	—
Splenic node	0.5	0.6	2.5
Hepatic node	0	0.6	3.4

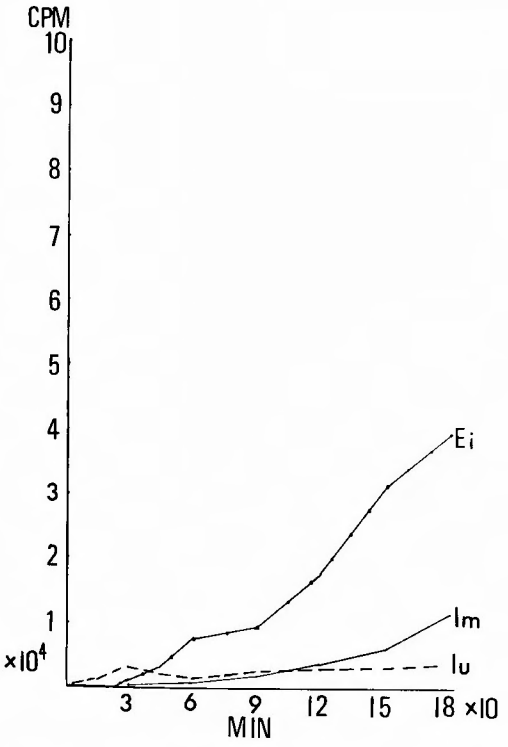

Fig. 13 Radioactivity in thoracic duct lymph following injection of RIHSA into the esophagus after ligation of the azygos and the intercostal veins.

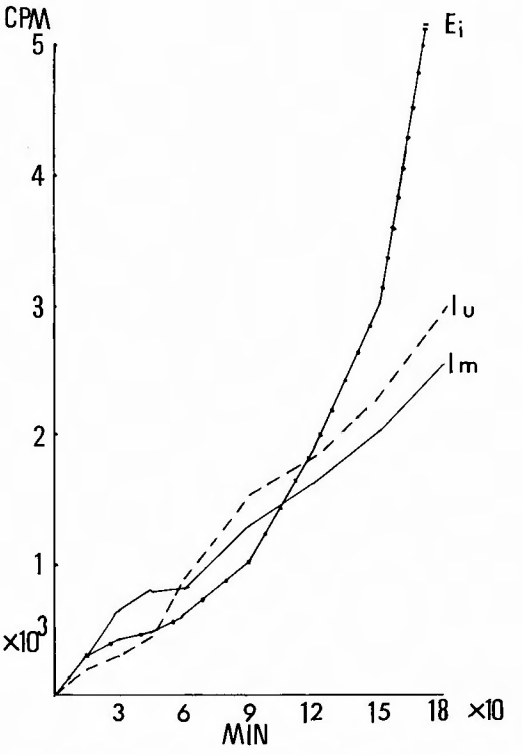

Fig. 14 Radioactivity in venous blood following injection of RIHSA into the esophagus after ligation of the azygos and the intercostal veins.

7. Experiments with RIHSA injection following transection of the esophagus.

Following thoracotomy in the sixth intercostal space, the esophagus was transected at the height of the bifurcation and both stumps of the esophagus were fastened to each other to prevent them from retracting. Fifty μc of RIHSA was injected into the proximal or distal portions of the esophagus. Then, the counts per minute both in the thoracic

Table 15 Radioactive values following RIHSA injection into the transected esophagus (CPM)

Dog No. and injection site	Radioactivity in thoracic duct lymph		Radioactivity in venous blood	
Min.	85 Proximal	86 Distal	85 Proximal	86 Distal
15	754	584	590	342
30	600	362	997	440
45	558	281	1190	638
60	702	438	1532	817
90	976	886	1883	933
120	2694	1221	2427	1088
150	4400	1385	2730	1195
180	7987	2143	3680	1150

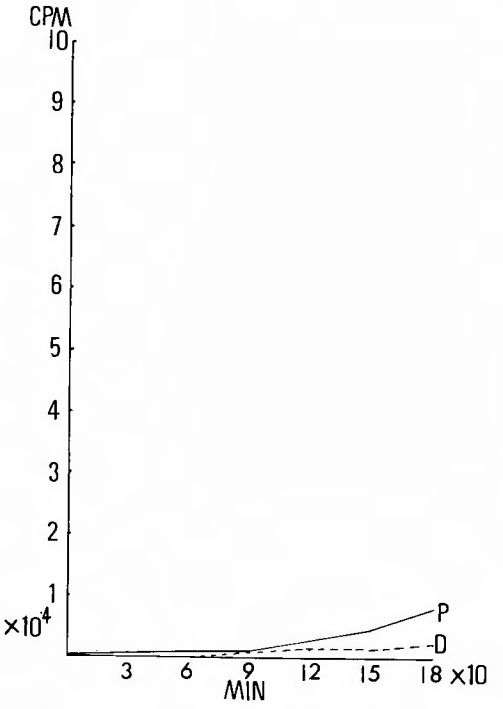

Fig. 15 Radioactivity in thoracic duct lymph following RIHSA injection into proximal (P) or distal (D) portion of the transected esophagus.

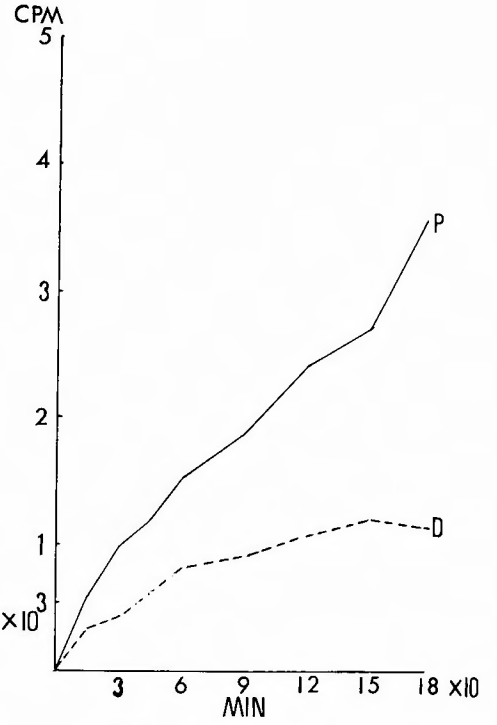

Fig. 16 Radioactivity in venous blood following RIHSA injection into proximal (P) or distal (D) portion of the transected esophagus.

Table 16 Distribution of radioactivity following RIHSA injection into the transected esophagus

Specimen \ Dog No. and injection site	Per cent count	
	85 (Proximal)	86 (Distal)
Injection site	100	100
Right retropharyngeal node	0	0
Left retropharyngeal node	0	0
Left deep cervical node	0.7	—
Superior mediastinal node	5.0	0.2
Paratracheal node	—	1.8
Right tracheobronchial node	0.3	0.3
Middle tracheobronchial node	5.0	2.0
Left tracheobronchial node	0.4	5.2
Nodes along the left gastric artery	0	0
Splenic node	0	0
Hepatic node	0	0

duct lymph and in the venous blood were measured. When the distal portion of the transected esophagus was injected, radioactivities in the thoracic duct lymph and venous blood showed remarkably lower values as compared with those of the proximal one (Tab.

15, Fig. 15 and 16). Transection of the esophagus will give rise to stagnation of lymph in the distal portion, which can be presumed from the data of per cent count of the regional lymph nodes. (Tab. 16).

DISCUSSION

There are some differences in the relationship among the cervical, thoracic or abdominal portions of the esophagus and the thoracic duct. It is obviously derived from the anatomical site, respiratory movement, pressure in the thorax, movement of the gastrointestinal tract, food consumption, etc.

When the lymph nodes in the upper abdomen were removed, the appearance of I^{131}-albumin in the thoracic duct lymph decreased, but that in venous blood increased 1 to 2 weeks after operation. This result shows that the dissection of lymph nodes without radical removal of cancer cells facilitates the hematogenous dissemination. Usually, the functioning straight-line unobstructed lymphatic channels are able to assume a load up to a critical point. When this limit is reached, accessory communications may begin to function and provide return routes for the overload. These accessory communications may be lymphatico-venous or lymphatico-lymphatic[37)42)]. The development of the former seems to occur within a short time, while that of the latter needs about 3 weeks before it begins to function. Obstruction of lymphatic channels due to dissection of lymph nodes encourages the function of lymphatico-venous communication.

Ligation of the left gastric artery with lymph node dissection in the upper abdomen gave a similar result as found after the removal of the lymph nodes alone 2 weeks after the procedures. However, RIHSA in the thoracic duct lymph increased remarkably 3 weeks after the procedures. No remarkable increase was observed in radioactive values in venous blood. It is doubtful how contributive the ligation alone is to form new communications in such animals as dogs, having a rich network of blood vessels. There is no doubt, however, that the lymphatico-lymphatic collaterals must have developed and regenerated the communication with the thoracic duct 3 weeks after these operations. Following the performance of a radical dissection for cancer and especially if there is lymphatic blockage from metastases, the resulting prevalent alteration in lymphatic dynamics is aggravated. In addition to the escape of lymph into the free tissue spaces, with the possibility of seeding of cancer cells in these spaces, the sealing-off of the severed lymphatic vessels produces a serious obstruction to lymphatic flow. If a collateral circulation develops, it is possible for cancer cells resident within the intervening lymphatic tissue spaces to transverse great distances throughout the body by means of the newly formed collateral lymphatic circulation.[4)].

Radioactivities in thoracic duct lymph decreased after paraffin-blockade of lymphatics in the esophageal wall. Per cent count of the regional lymph nodes under paraffin-blockade suggested a possibility of lodgment of atypical metastases. Neoplastic or inflammatory infiltration and obliteration of lymphatic vessels, with or without invasion of the thoracic duct, blocks normal lymph flow, impairs absorption of foodstuff, interferes with drainage of splanchnic interstitial fluid[5)14)]. The reduction of lymph flow may derive from the destruction of lymph channels and emboli of tumor cells in the perivascular lymphatics.

The lymphatic capillary in the mucosa extends complicatedly throughout the length

of the esophagus, but in the submucosa it runs considerable distances in a longitudinal fashion and at successive levels transport the lymph to the regional nodes. On the other hand, the lymphatic capillary in the muscle layers of the esophagus flows directly into the regional nodes[24)31)34)].

The lymph flow in the esophageal wall has a pronounced tendency to spread longitudinally about 6 times more than transversally[15)34)]. In the primary tumor of the esophago-cardiac junction, the cancer showed a more evident tendency to extend proximally than distally[7)33)41)46)49)]. Therefore, it is emphasized that a longer, especially, proximal portion of the esophagus should be removed as much as possible during the operation[21)36)].

Case 1. A male aged 64.

Subtotal esophagectomy was carried out for carcinoma of the midthoracic esophagus. The findings at surgery were as follows : S 2, N 3, CAT Ⅲ, SAT Ⅲ, and INF γ. There was a pea-sized metastasis in the submucous layer of the cervical esophagus far from the primary tumor of squamous cell carcinoma (Fig. 17). This is a clear-cut example of the tendency for carcinoma of the esophagus to extend considerable distances longitudinally by way of the submucosal lymphatics[3)30)36)47)].

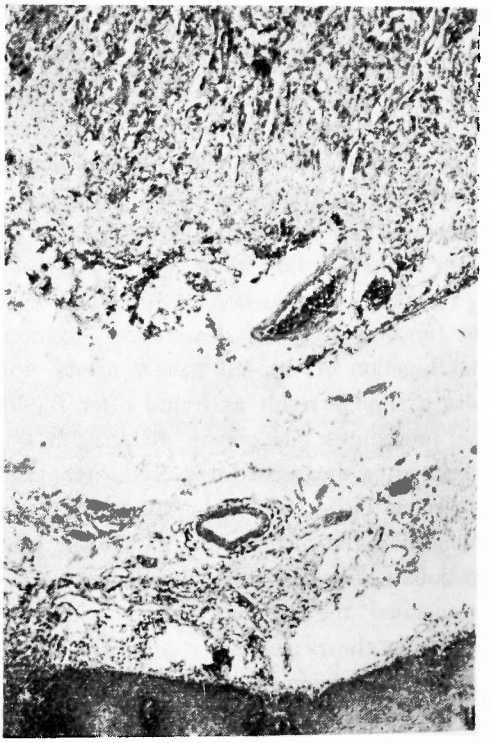

Fig. 17 Case 1 shows carcinoma in the submucosal lymphatics in the cervical portion of the esophagus.

As a rule, cancers of the pharynx, the cervical esophagus and cardiac region have a definite tendency to spread to regional lymph nodes, whereas carcinoma of the thoracic esophagus have not a definite tendency of regional lymph node metastasis[32)]. It can be seen, however, from the data of paraffin-blockade series that a retrograde or unusual lymphatic dissemination may be established with ease. Moreover, preoperative radiotherady tends to facilitate the atypical remote lymph node metastasis due to the devasation of normal lymphatics[2)]. Even if a primary tumor locates in the thoracic esophagus, we should keep an eye on infiltration of the lymph nodes in the cervical region or under the diaphragm[29)48)], particularly after preoperative radio-therapy.

Radical removal of cancer of the thoracic esophagus is usually accompanied with vagotomy and sometimes severance of the azygos vein.

Division of the vagal nerves result in significant reduction of peristaltic activity and blood flow of the intestine due to the opening of submucosal arterio-venous shunts[39)]. Alterations in mesothelial permeability have also been demonstrated following vagotomy and this may account for some of the edema seen in tissue sections of the small intestine in experimental animals[6)]. These factors may cause a decrease in lymph flow in the

thoracic duct following vagotomy. On the other hand, tonus of the lymph vessels does not take a significant part in lymphatic circulation[25]. For instance, endotoxin shock was associated with an immediate systemic hypotension, a fall in central venous pressure, a decrease in blood volume, nevertheless there was an increase in thoracic duct lymph flow[26]. It is difficult to draw an obvious conclusion about the appearance of RIHSA in thoracic duct lymph or venous blood following vagotomy, since it will complicatedly influence the lymph flow of the dependent organs and tissues.

Ligation of the azygos and the intercostal veins resulted in reduction of the appearance of I^{131}-albumin both in thoracic duct lymph and in venous blood following injection into the mid- or lower thoracic portions of the esophagus, which might be under the most intensive influence. The rate of removal of I^{131}-albumin from the tissue is significantly reduced in edema caused by lymphatic obstruction, but significantly increased in edema caused by venous obstruction, congestive heart failure or hypoproteinemia[19][37]. However, in the series of obstruction of the azygos and the intercostal veins, these results may be influenced by the duration of the experiment for only 3 hours, and venous return through extensive collateral vessels.

High ligation of the veins draining from a primary tumor was advocated to avoid the possible spread to other organs during surgery of the carcinoma[10]. However, such a procedure may lead to the increasing occurrence of malignant cells in the systemic circulation via a retrograde flow of venous circulation along the intrinsic and marginal veins[35]. Anyway, ligation of the azygos and the intercostal veins seems to be effective to avoid the liberation of tumor cells into systemic circulation. It is debatable to assess the prognostic implication of malignant cells liberated during the surgical manipulation[43]. It is better to avoid such risks as iatrogenic transport of the malignant cells into the systemic circulation because of the increasing number of tumor cells in venous blood[11]. The presence of circulating cells, however, does not necessarily signify the establishment of metastases[17][35], and occurrence of metastases will, of course, depend upon the viability of cancer cells, their ability to establish metastases, and resistance of the patients themselves[35][38].

Fig. 18 Lymphangiography of the thoracic duct demonstrating the communication to the right lymphatic duct.

During the esophagectomy, transection of the esophagus is a method of choice to make this procedure easy and avoid occurrence of bilateral thoractomy.

It is clear from the data that transection of the esophagus proximal to the tumor is better to avoid liberation of malignant cells

into lymphatic or blood vessel. If the esophagus is transected distal to the tumor, the esophagus proximal to the tumor should be ligated to reduce the number of tumor cells both within the lumen and the systemic circulation. It is natural that lymph flow in the thoracic duct may be changed by compression or infiltration of tumor. In addition to thoracic duct lymph, about 10% of total lymph return in the dog is carried by the right lymphatic duct[26]. Cannulation into the thoracic duct at the height of the ninth intercoatal region following thoracotomy was carried out one week after ligation of the thoracic duct at the jugular-subclavian vein junction. Popiodols was injected constantly at a rate of 0.185 ml per minute (total volume : 5 ml) using a special injector, and films were taken immediately. Figure 18 shows the remarkable communication between the right lymphatic and the thoracic duct. This fact suggests that the lymph nodes in the right supra-clavicular region is often invaded easily in the course of advanced esophageal cancer.

Case 2. A male aged 65.

This patient had undergone intrathoracic esophagogastrostomy following left transthoracic resection of the lower esophagus and cardia for cancer of the esophagocardiac region. Five months later, postmortem examination showed metastases at the right deep cervical lymph nodes only. In this case, only metastases at the paraesophageal nodes in the lower thoracic portion were found during the operation (Fig. 19).

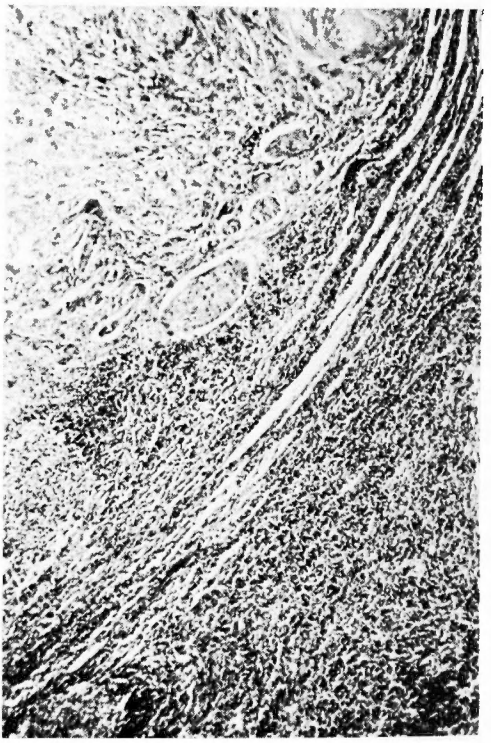

Fig. 19 Case 2 shows massive cancer infiltration in the right deep cervical lymph node.

The lymphangiography of the thoracic duct demonstrated abnormal findings in 55% of the cases of esophageal carcinoma, and it was impossible for all such patients to undergo radical operation[20]. This coincides with the number of non-resectability of the carcinoma of the esophagus[2]. Thus, the thoracic duct is in danger of early invasion of cancer of the esophagus[44].

As may be seen from what has been stated above, results of treatment for esophageal cancer have been poor and discouraging. However, we should challenge this neoplasm by means of more advanced procedures for diagnosis and treatment.

SUMMARY

RIHSA was injected into the esophagus in dogs from the various points of view. The appearance of radioactivities in thoracic duct lymph, venous blood, and lymph nodes were studied.

The results were as follows :

1) Considering the lymphatics of the esophagus, the cervical esophagus seems to

have a close relation with the lymph nodes even in the upper thoracic portion except for regional nodes, and the esophagus in the thorax has connection with all regional nodes of the thorax, but the nodes in the upper abdomen receive lymph from the lower thoracic portion of the esophagus. The lymphatics of the abdominal esophagus also have relation with the nodes in the thoracic cavity, especially at the tracheal bifurcation.

2) Removal of the lymph nodes in the upper abdomen caused RIHSA from the abdominal esophagus to deliver more into venous blood than into thoracic duct lymph 2 weeks after the experimental procedure.

3) Ligation of the left gastric artery with removal of lymph nodes in the upper abdominal region produced remarkable diminution of appearance of RIHSA in thoracic duct lymph and preponderant appearance in venous blood 2 weeks after the experimental procedure. On the contrary, radioactivity in thoracic duct lymph significantly increased after 3 weeks. The per cent count of the lymph nodes exhibited zero 2 weeks, but a high per cent count 3 weeks after the procedure.

4) Paraffin-blockade of the lymphatics in the esophagus prevented I^{131}-albumin from flowing into the thoracic duct and delivered it into venous blood. It shows the possible development of retrograde or collateral lymphatic channels.

5) Vagotomy at the height of the tracheal bifurcation resulted in a marked reduction of the radioactivity in thoracic duct lymph following injection of RIHSA into the same level of the esophagus, and a slight increase following injection into the lower thoracic esophagus. The activity of RIHSA in venous blood tended to fall below that of the control. The definite conclusions, however, cannot be drawn from these data.

6) Ligation of the azygos and the intercostal veins caused reduction of the appearance of RIHSA both in thoracic duct lymph and in venous blood.

7) The appearance of RIHSA from the distal segment of the transected esophagus was significantly reduced both in thoracic duct lymph and in venous blood.

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和文抄録

外科的立場からみた食道リンパ系に関する実験的研究

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食道癌手術の根治性を妨げる原因の一つにリンパ節転移や粘膜下転移の問題がある．そこで食道リンパ系の特異性を外科的立場から実験的に追求，検討してみた．

1)　食道壁内リンパ系と胸管および所属リンパ節との関係を追求するために，成犬で胸管ドレナージを行なつた後，頸部および胸部食道壁にRIHSA－50 μc を食道鏡直視下で注射器を用いて注入した．胸管リンパ液を3時間にわたつて経時的に採取し，その各1 mlの放射能値をscintillation counterを用いて測定した．脱血死せしめた後，採取した各所属リンパ節の放射能値を，RIHSA注入部食道1 gのそれに対する%カウントをもつて示した．

2)　腹腔内リンパ節郭清や左胃動脈結紮が食道リンパ系におよぼす影響について検討するために，成犬の上腹部リンパ節を郭清して1～2週間後に腹部食道壁にRIHSAを注入した．さらに左胃動脈結紮を追加した実験犬で2～4週間後に同様の実験を行なつた．

3)　食道癌が壁内リンパ流におよぼす変化を追求するために，成犬で融解したparaffin（融点：42°C）を食道鏡直視下で胸部食道壁に注入した．2週間後にparaffin block部の尾側食道壁にRIHSAを注入した．

4)　食道癌手術に伴なう胸腔内迷走神経切断が食道リンパ系におよぼす影響について検討するために，成犬でrespiratorを用いて開胸し，気管分岐部の高さで両側迷走神経を切断した．そのほぼ同じ高さの食道壁および下胸部食道壁にRIHSAを注入した．

5)　奇静脈切断が食道リンパ系におよぼす影響を検討するために，成犬で奇静脈が上大静脈に流入する部位から，第10肋間に至る左右肋間静脈をすべて結紮した後，胸部食道壁にRIHSAを注入した．

6)　食道離断に伴なう食道壁内リンパ流の変化を追求するために，成犬で気管分岐部の高さで食道を離断し，その頭側および尾側食道壁にRIHSAを注入した．

以上，各実験について胸管リンパ，大腿静脈血および所属リンパ節の放射能値を測定した結果，次のような結論を得た．

1)　頸部食道は，大体上胸部リンパ節まで，胸部食道はすべての胸腔内リンパ節に，とくに下胸部食道は上腹部リンパ節に，また腹部食道は胸腔内，ことに気管分岐部リンパ節と密接な関係をもつていた．

2)　上腹部リンパ節郭清後2週間では，腹部食道壁に注入したRIHSAは胸管リンパより静脈血中に排出されやすくなつた．さらに左胃動脈結紮を追加した実験では，2週間後で胸管へのRIHSA流出は著減し，3週間後では著しい増加を認めた．所属リンパ節の放射能値百分比は，2週間後ではすべて0であつたが，3週間以後では多量の放射能値を検出することができた．

3)　食道壁内リンパ流を阻害すると，食道より胸管へのRIHSA流出は停滞し，静脈血へより流出しやすくなり，同時に遠隔部リンパ節に多量の放射能値が検出できるようになつた．

4)　胸腔内迷走神経切断は，対照例と比較して食道リンパ系になんらかの影響をおよぼすことが推察されたが，一定の傾向を結論ずけることはできなかつた．

5)　奇静脈および肋間静脈を結紮すると，食道より胸管リンパおよび静脈血へのRIHSA流出はともに減少する傾向を示した．

6)　食道を離断すると，その尾側食道から胸管リンパおよび静脈血へのRIHSA流出はともに著しく阻害された．

すなわち食道癌手術で奇静脈切断や，癌腫の頭側で食道離断を行なえば，術中腫瘍細胞の循環系への流出を防ぐ意味で有効であると考えられる．